A New Radiation Concept, Treatment of Squamous Cell Carcinoma by Alpha-radiation Based Brachytherapy (Alpha DaRT)

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Abstract

Purpose/Objective(s): The first clinical trial in humans with skin and oral cavity squamous cell carcinomas was performed in order to evaluate the effect of a unique intratumoral alpha radiation based tumor ablation treatment termed Diffusing Alpha Emitter Radiation Therapy (DaRT).

Materials/Methods: Radon-224 loaded sources (DaRT seeds) were inserted into solid tumors and released by recoil short-lived alpha-emitting atoms (Ra-220, Po-216, Pb-212, Bi-212, Po-212, Pb-212, Ir-212). These atoms disperse in the tumor, and spray it with highly destructive alpha radiation. The decay products diffuse into the tumor mass to a distance of at least 5 mm.

Results: A feasibility and safety clinical study is ongoing and currently were treated 14 patients at the Rabin Medical Center (Israel). Patients with gamma radiation resistant recurrent histopathological confirmed skin or head and neck SCC, and tumor size ≤ 5 centimeters in the longest diameter, were enrolled. Treatment was delivered based on a CT-simulation pre-treatment plan. The seeds (1 cm long and 0.5 mm in diameter) each carrying a dose of 2 μC were placed 6 millimeters from each other. CT was used to check the position of the radioactive seeds. Two to four weeks after implantaion the seeds were removed, and six weeks after treatment CT was performed to assess the effect of treatment. The Age of the patients ranged between 70 to 94 (median 81). Seven patients had recurrent oral cavity SCC and seven diagnosed with aggressive skin SCC. All were treated within radiation failure fields (Rashkind dosage 740 Gy). All tumors responded to the treatment: 9 tumors had a complete response; four tumors showed a partial response, and one tumor is still under observation. No major toxicity was noted.

Conclusion: In this feasibility and safety human study we demonstrated that alpha particle based DaRT exhibit enhanced radiobiological potential. The treatment was effective against radio-resistant SCC tumors without major toxicity.

Key Inclusion Criteria

- Histopathological confirmation of SCC
- Lesions ≤ 5 cm in the longest diameter (without nodal spread)
- Age ≥ 18
- WOCBP will have evidence of negative pregnancy test
- Life expectancy ≥ 6 months
- ECOG ≤ 2

Key Exclusion Criteria

- Ulcerative lesions
- Tumor of Keratoacanthoma histology
- Patients with membranous diseases, autoimmune diseases or vasculitis.
- Patients under immunosuppressive or anti-contrasen treatment
- Participation in other studies in the past 30 days

Clinical Study

Eligibility Criteria

Response to DaRT

Patient Age Tumor Location Previous RT Response
1 87 Sub-Mandibular + Mandible Yes Partial
2 80 Ear Yes Complete
3 94 Tongue Yes (C2) Complete
4 80 Lip Yes Partial
5 75 Parotid Yes Partial
6 94 Tongue Yes Complete
7 69 Nasal Yes Complete
8 81 Ear Yes Complete
9 91 Tongue Yes Complete
10 76 Cheek No Complete
11 78 Lip Yes Complete
12 70 Forehead No Partial
13 66 Lip No Complete
14 88 Parotid Yes Unknown

Potent α radiation: Extensively damages the DNA

α radiation - Radiates the DNA
α radiation - Directly damages the DNA
α radiation - Deposition on oxygen process
α radiation - Breakdown of oxygen process
α radiation - Reparable single-strand breaks
α radiation - Unreparable double-strand breaks

Safety

Radioactivity Levels: Urine Measurements

Radioactivity Levels: Blood Measurements

Conclusions

Treatment plan

- The ideal planning should include radiationist, surgeon and physicist
- The planning should be based on both direct visualization and imaging
- Better understanding of the required dose and radiation distribution will improve outcomes in large tumors
- Low Toxicity better over cover than under!!

The Procedure

- The procedure is feasible, simple and can be done in relatively short time

The Alpha DaRT Treatment

- The treatment has very low toxicity and overall seems to be safe
- The treatment was proven to have the ability to destroy SCC tumors
- Complete Response over 70%!!